09/833111

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PATENT
Customer No. 22,852
Attorney Docket No. 6832.0014

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No.: 6,946,134 B1)
)
Inventors:)
)
Craig A. Rosen and William A. Haseltine)
)
Issue Date.: September 20, 2005)
)
For: ALBUMIN FUSION PROTEINS)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REQUEST FOR CERTIFICATE OF CORRECTION

Pursuant to 35 U.S.C. §§ 254 and 255, and 37 C.F.R. §§ 1.322 and 1.323, this is a request for a Certificate of Correction in the above-identified patent. Some of the mistakes identified in the appended Form occurred through the fault of the Patent Office, as clearly disclosed by the records of the application which matured into this patent.

For example, the priority claims to Provisional Application Nos. 60/256,931, filed December 21, 2000; 60/199,384, filed April 25, 2000; and 60/229,358, filed April 12, 2000, were deleted in an Amendment filed June 3, 2004, and a Corrected Filing Receipt reflecting the change was mailed by the PTO on June 21, 2004. However, the issued patent was printed with the priority claims in the title page under item (60) and in the first paragraph of the specification.

Furthermore, reference WO 97/24445 was both cited by Applicants in an Information Disclosure Statement filed May 18, 2004, and also by the Office in an Office Action dated August 20, 2003. In both instances, the publication date of the reference was listed as 07/10/97. However, on page 2, column 1, of the issued patent, the reference indicated by an asterisk as having been cited by the Office is listed with a publication date of 10/1997. The Certificate of Correction corrects the publication date to 7/1997.

The omitted reference WO 98/49296 under item (56) (References Cited) in the title page, was also submitted in a Supplemental Information Disclosure Statement filed May 18, 2004, in accordance with the provisions of 37 C.F.R. § 1.97 and 37 C.F.R. § 1.98. Under MPEP 609, "[o]nce the minimum requirements of 37 CFR 1.97 and 37 CFR 1.98 are met, the examiner has an obligation to consider the information." Because WO 98/49296 was submitted in conformance with the rules, WO 98/49296 should have been listed under item (56) (References Cited) in the title page.

Moreover, none of the corrections made to SEQ ID NOs in the specification by an Amendment filed on May 18, 2004, were incorporated into the issued patent. Similarly, the issued patent reflects the original Sequence Listing filed rather than the Substitute Sequence Listing submitted on May 18, 2004. The Sequence Listing in the attached Certificate of Correction is identical to the Substitute Sequence Listing filed on May 18, 2004, and is also identical to the computer readable copy of the Substitute Sequence Listing also submitted on May 18, 2004. Thus, the correction contains no new matter.

Finally, the issued patent was printed with the claims presented in an Amendment dated November 20, 2003, rather than the claims that were allowed in a Notice of Allowance dated February 20, 2004, and July 20, 2004. In both Notice of Allowances, claims 1-21 and 26-29 were found allowable based on an Examiner's Amendment of February 20, 2004, which was authorized by Applicants' representative in a telephone interview on February 6, 2004. Although claim 19 appears to have been inadvertently omitted from the Examiner's Amendment of February 20, 2004, claim 19 was never canceled and both Notice of Allowances clearly indicate that claims 1-21 and 26-29 were allowable.

Other mistakes identified in the appended Form are of a clerical or typographical nature, or of minor character, and resulted from an error made in good faith by patentees. A check in the amount of $100 (the fee set forth in 37 C.F.R. § 1.20(a)) is attached. Should a check not be appended or should any additional fees be needed, authorization is hereby given to charge any fees due in connection with the filing of this request to Deposit Account No. 06-0916.

Two (2) copies of PTO Form 1050 are appended. The complete Certificate of Correction involves thirty-nine (39) pages. Issuance of the Certificate of Correction containing the correction is earnestly requested.

Please charge any required fees not included herewith to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 19, 2005

By: Charles E Van Horn
Charles E. Van Horn
Reg. No. 40,266

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. 6,946,134 B1 Page 1 of 39

APPLICATION NO.: 09/833,111

ISSUE DATE: September 20, 2005

INVENTOR(S): Craig A. Rosen, William A. Haseltine

It is hereby certified that an error or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Under item (60) (Related U.S. Application Data) of the title page, delete the text beginning with "Provisional application No. 60/256,931" to and ending "provisional application No. 60/229,358, filed on Apr. 12, 2000."

Under item (57) (ABSTRACT) of the title page, "disordrs" should read --disorders--.

On page 2, column 1, in the 8th reference from the bottom, "WO WO97/24445 *10/1997" should read --WO WO 97/24445 *7/1997--.

Under item (56) (References Cited) of the title page and under FOREIGN PATENT DOCUMENTS beginning on page 1, insert --WO WO 98/49296 5/1998--.

On page 2, column 2, in the 10th reference under OTHER PUBLICATIONS (Armstrong, J.D., et al.,), "(199)" should read --(1990)--.

On page 3, column 2, in the 13th reference (Bian, Z., et al.,), "78:355-344" should read --78:335-344--.

On page 4, column 1, in the 4th reference (Bolognesi, D.P., et al.,), "1233-1234" should read --246(4935):1233-1234--.

On page 5, column 1, in the 9th reference (Cunningham, B.C. et al.,), "245:821-825" should read --254:821-825--.

On page 5, column 1, in the 15th reference (Dedieu, J-F., et al.,), "*Journal of Virogy*" should read --*Journal of Virology*--.

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U.S. Patent No. 6,946,134

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DEC 2 1 2005

On page 9, column 1, in the 17th reference (Lewis, C., et al.,), "Dysfunctoin" should read --Dysfunction--.

On page 12, column 2, in the 17th reference, "Simoes, S., et a.," should read --Simoes, S., et al.,--.

On page 13, column 1, in the 11th reference, "Sotomayer" should read --Sotomayor--, and "77:19-16" should read --77:19-26--.

On page 14, column 1, in the 9th reference (Vorumn, H., et al.,), "19:1793-1802" should read --*Electrophoresis* 19:1793-1802--.

In the Specification:

Col. 1, line 3, delete the text beginning with "This application" to and ending "in its entirety." in col. 1, line 8.

Col. 267, line 18, "NO:36)." should read --NO:72).--.

Col. 418, line 33, "ID NO: 36)" should read --ID NO: 73)--.

Col. 439, line 24, "(SEQ ID NO: 37)" should read --(SEQ ID NO: 74)--.

Col. 440, line 46, "(SEQ ID NO: 38)" should read --(SEQ ID NO: 75)--.

Col. 440, line 50, "39)" should read --76)--.

Col. 440, line 67, "NO: 40)" should read --NO: 77)--.

Col. 443, line 5, "(SEQ ID NO: 41)" should read --(SEQ ID NO: 78)--.

Col. 443, line 7, "(SEQ ID NO: 42)" should read --(SEQ ID NO: 79)--.

Col. 445, line 24, "(SEQ ID NO: 43)" should read --(SEQ ID NO: 80)--.

Col. 445, line 29, "(SEQ ID NO: 44)" should read --(SEQ ID NO: 81)--.

Col. 445, line 34, "ID NO: 39)" should read --ID NO: 76)--.

Col. 445, line 50, "(SEQ ID NO: 45)" should read --(SEQ ID NO: 82)--.

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In the Claims:

Cancel claims 1-25, and insert the following claims:

1. An albumin fusion protein comprising a member selected from the group consisting of:

(a) a cerebus protein and albumin, wherein albumin comprises the amino acid sequence of SEQ ID NO:18;

(b) a cerebus protein and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf life of the cerebus protein compared to the shelf-life of the cerebus protein in an unfused state;

(c) a cerebus protein and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf life of the cerebus protein compared to the shelf-life of the cerebus protein in an unfused state, and further wherein the said fragment comprises the amino acid residues 1-387 of SEQ ID NO:18;

(d) a fragment of a cerebus protein and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment has a biological activity of the cerebus protein;

(e) a cerebus protein, or fragment thereof and albumin, or fragment thereof, of (a) to (d), wherein the cerebus protein, or fragment thereof, is fused to the N-terminus of albumin or the N-terminus of the fragment of albumin;

(f) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), wherein the cerebus protein or fragment thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment of albumin;

(g) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), wherein the cerebus protein or fragment thereof, is fused to the N- terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment of albumin;

(h) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), which comprises a first cerebus protein or fragment thereof and a second cerebus protein or fragment thereof, wherein said first cerebus protein or fragment thereof is different from said second cerebus protein or fragment thereof;

(i) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (h), wherein the cerebus protein or fragment thereof, is separated from the albumin or the fragment of albumin by a linker; and

(j) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (i), wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

and further wherein R1 is cerebus protein or fragment thereof, L is linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or a fragment of albumin.

2. The albumin fusion protein of claim 1, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the cerebus protein or fragment thereof, in an unfused state.

3. The albumin fusion protein of claim 1, wherein the in vitro biological activity of the cerebus protein or fragment thereof, fused to albumin, or fragment thereof, is greater than the in vitro biological activity of the cerebus protein or fragment thereof, in an unfused state.

4. The albumin fusion protein of claim 1, wherein the in vivo biological activity of the cerebus protein or fragment thereof, fused to albumin, or fragment thereof, is greater than the in vivo biological activity of the cerebus protein or fragment thereof, in an unfused state.

5. An albumin fusion protein comprising a cerebus protein or fragment thereof, inserted into an albumin, or fragment thereof, comprising the amino acid sequence of SEQ ID NO:18 or fragment thereof.

6. An albumin fusion protein comprising a cerebus protein or fragment thereof, inserted into an albumin, or fragment thereof, comprising an amino acid sequence selected from the group consisting of:

(a) amino acid residues 54 to 61 of SEQ ID NO:18;
(b) amino acid residues 76 to 89 of SEQ ID NO:18;
(c) amino acid residues 92 to 100 of SEQ ID NO:18;
(d) amino acid residues 170 to 176 of SEQ ID NO:18;
(e) amino acid residues 247 to 252 of SEQ ID NO:18;
(f) amino acid residues 266 to 277 of SEQ ID NO:18;
(g) amino acid residues 280 to 288 of SEQ ID NO:18;
(h) amino acid residues 362 to 368 of SEQ ID NO:18;
(i) amino acid residues 439 to 447 of SEQ ID NO:18;
(j) amino acid residues 462 to 475 of SEQ ID NO:18;
(k) amino acid residues 478 to 486 of SEQ ID NO:18; and
(l) amino acid residues 560 to 566 of SEQ ID NO:18.

7. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the shelf-life of the cerebus protein or fragment thereof, as compared to the shelf-life of the cerebus protein or fragment, in an unfused state.

8. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the shelf-life of the cerebus protein or fragment thereof, as compared to the shelf-life of the cerebus protein or fragment, in an unfused state.

9. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vitro biological activity of the cerebus protein or fragment thereof, fused to albumin as compared to the in vitro biological activity of the cerebus protein or fragment, in an unfused state.

10. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vitro biological activity of the cerebus protein or fragment thereof, fused to albumin as compared to the in vitro biological activity of the cerebus protein or fragment, in an unfused state.

11. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vivo biological activity of the cerebus protein or fragment thereof, fused to albumin compared to the in vivo biological activity of the cerebus protein or fragment, in an unfused state.

12. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vivo biological activity of the cerebus protein or fragment thereof, fused to albumin compared to the in vivo biological activity of the cerebus protein or fragment, in an unfused state.

13. The albumin fusion protein of any one of claims 1-12, which is non-glycosylated.

14. The albumin fusion protein of any one of claims 1-12, which is expressed in yeast.

15. The albumin fusion protein of claim 14, wherein the yeast is glycosylation deficient.

16. The albumin fusion protein of claim 14, wherein the yeast is glycosylation and protease deficient.

17. The albumin fusion protein of any one of claims 1-12, which is expressed by a mammalian cell.

18. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

19. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein further comprises a secretion leader sequence.

20. A composition comprising the albumin fusion protein of any one of claims 1-12 and a pharmaceutically acceptable carrier.

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21. A kit comprising the composition of claim 20.

22. A method of extending the shelf life of a cerebus protein or fragment thereof, comprising the step of fusing the cerebus protein or fragment thereof, to albumin, or fragment thereof, sufficient to extend the shelf-life of the cerebus protein or fragment thereof, compared to the shelf-life of the cerebus protein, or fragment thereof in an unfused state.

23. A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-12.

24. A vector comprising the nucleic acid molecule of claim 27.

25. A host cell comprising the nucleic acid molecule of claim 28.

In the Sequence Listing:

Delete the Sequence Listing beginning in Col. 465, beginning with the text "<160> NUMBER OF SEQ ID NOS: 72" to and ending "<400> SEQUENCE: 72

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   1               5                  10                  15"
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in Col. 505 and insert the following Sequence Listing:

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<221> primer_bind
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<221> primer_bind
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<211> 16
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<212> DNA
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ac 62

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<222> (1)..(1755)

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1 5 10 15

gaa aat ttc aaa gcc ttg gtg ttg att gcc ttt gct cag tat ctt cag 96
Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
20 25 30

cag tgt cca ttt gaa gat cat gta aaa tta gtg aat gaa gta act gaa 144
Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
35 40 45

ttt gca aaa aca tgt gtt gct gat gag tca gct gaa aat tgt gac aaa 192
Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
50 55 60

tca ctt cat acc ctt ttt gga gac aaa tta tgc aca gtt gca act ctt 240
Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65 70 75 80

cgt gaa acc tat ggt gaa atg gct gac tgc tgt gca aaa caa gaa cct 288
Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
85 90 95

```
gag aga aat gaa tgc ttc ttg caa cac aaa gat gac aac cca aac ctc   336
Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
            100                 105                 110

ccc cga ttg gtg aga cca gag gtt gat gtg atg tgc act gct ttt cat   384
Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
        115                 120                 125

gac aat gaa gag aca ttt ttg aaa aaa tac tta tat gaa att gcc aga   432
Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
    130                 135                 140

aga cat cct tac ttt tat gcc ccg gaa ctc ctt ttc ttt gct aaa agg   480
Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145                 150                 155                 160

tat aaa gct gct ttt aca gaa tgt tgc caa gct gct gat aaa gct gcc   528
Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
                165                 170                 175

tgc ctg ttg cca aag ctc gat gaa ctt cgg gat gaa ggg aag gct tcg   576
Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
            180                 185                 190

tct gcc aaa cag aga ctc aaa tgt gcc agt ctc caa aaa ttt gga gaa   624
Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
        195                 200                 205

aga gct ttc aaa gca tgg gca gtg gct cgc ctg agc cag aga ttt ccc   672
Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
    210                 215                 220

aaa gct gag ttt gca gaa gtt tcc aag tta gtg aca gat ctt acc aaa   720
Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225                 230                 235                 240

gtc cac acg gaa tgc tgc cat gga gat ctg ctt gaa tgt gct gat gac   768
Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
                245                 250                 255

agg gcg gac ctt gcc aag tat atc tgt gaa aat cag gat tcg atc tcc   816
Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
            260                 265                 270

agt aaa ctg aag gaa tgc tgt gaa aaa cct ctg ttg gaa aaa tcc cac   864
Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
        275                 280                 285

tgc att gcc gaa gtg gaa aat gat gag atg cct gct gac ttg cct tca   912
Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
    290                 295                 300
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tta gct gct gat ttt gtt gaa agt aag gat gtt tgc aaa aac tat gct   960
Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305                 310                 315                 320

gag gca aag gat gtc ttc ctg ggc atg ttt ttg tat gaa tat gca aga   1008
Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
                325                 330                 335

agg cat cct gat tac tct gtc gtg ctg ctg ctg aga ctt gcc aag aca   1056
Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
            340                 345                 350

tat gaa acc act cta gag aag tgc tgt gcc gct gca gat cct cat gaa   1104
Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
        355                 360                 365

tgc tat gcc aaa gtg ttc gat gaa ttt aaa cct ctt gtg gaa gag cct   1152
Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
    370                 375                 380

cag aat tta atc aaa caa aac tgt gag ctt ttt gag cag ctt gga gag   1200
Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385                 390                 395                 400

tac aaa ttc cag aat gcg cta tta gtt cgt tac acc aag aaa gta ccc   1248
Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
                405                 410                 415

caa gtg tca act cca act ctt gta gag gtc tca aga aac cta gga aaa   1296
Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
            420                 425                 430

gtg ggc agc aaa tgt tgt aaa cat cct gaa gca aaa aga atg ccc tgt   1344
Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
        435                 440                 445

gca gaa gac tat cta tcc gtg gtc ctg aac cag tta tgt gtg ttg cat   1392
Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                 455                 460

gag aaa acg cca gta agt gac aga gtc aca aaa tgc tgc aca gag tcc   1440
Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                 470                 475                 480

ttg gtg aac agg cga cca tgc ttt tca gct ctg gaa gtc gat gaa aca   1488
Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
                485                 490                 495

tac gtt ccc aaa gag ttt aat gct gaa aca ttc acc ttc cat gca gat   1536
Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
            500                 505                 510
```

```
ata tgc aca ctt tct gag aag gag aga caa atc aag aaa caa act gca   1584
Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
        515                 520                 525

ctt gtt gag ctt gtg aaa cac aag ccc aag gca aca aaa gag caa ctg   1632
Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
    530                 535                 540

aaa gct gtt atg gat gat ttc gca gct ttt gta gag aag tgc tgc aag   1680
Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                 550                 555                 560

gct gac gat aag gag acc tgc ttt gcc gag gag ggt aaa aaa ctt gtt   1728
Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
                565                 570                 575

gct gca agt caa gct gcc tta ggc tta taacatctac atttaaaagc atctcag 1782
Ala Ala Ser Gln Ala Ala Leu Gly Leu
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<210> 18
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<212> PRT
<213> Homo Sapiens

<400> 18
Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
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Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
             20                  25                  30

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
         35                  40                  45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
     50                  55                  60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 65                  70                  75                  80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
                 85                  90                  95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
            100                 105                 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
        115                 120                 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
    130                 135                 140
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Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145                 150                 155                 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
                165                 170                 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
            180                 185                 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
        195                 200                 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
    210                 215                 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225                 230                 235                 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
                245                 250                 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
            260                 265                 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
        275                 280                 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
    290                 295                 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305                 310                 315                 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
                325                 330                 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
            340                 345                 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
        355                 360                 365

Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
    370                 375                 380

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385                 390                 395                 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
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Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
            420                 425                 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
        435                 440                 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                 455                 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                 470                 475                 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
                485                 490                 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
            500                 505                 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
        515                 520                 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
    530                 535                 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                 550                 555                 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
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Ala Ala Ser Gln Ala Ala Leu Gly Leu
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<210> 20
<211> 59
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<223> primer used in generation XhoI and ClaI
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site in pPPC0006

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<210> 21
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site in pPPC0006

<400> 21
tacaaactta agagtccaat tagc 24

<210> 22
<211> 29
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site in pPPC0006

<400> 22
cacttctcta gagtggtttc atatgtctt 29

<210> 23
<211> 60
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<223> Synthetic oligonucleotide used to alter restriction
sites in pPPC0007

<400> 23
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<210> 24
<211> 60
<212> DNA
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<221> Misc_Structure
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sites in pPPC0007

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<210> 25
<211> 32
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<210> 26
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<210> 27
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ctttaaatcg atgagcaacc tcactcttgt gtgcatcnnn nnnnnnnnnn nn 52

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<211> 24
<212> PRT
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<400> 29
Met Lys Trp Val Ser Phe Ile Ser Leu Leu Phe Leu Phe Ser Ser Ala
1 5 10 15

Tyr Ser Arg Ser Leu Asp Lys Arg
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<210> 30
<211> 114
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<223> forward primer useful for generation of PC4:HSA
albumin fusion VECTOR
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<223> Kozak sequence
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<223> cds natural signal sequence of human serum albumin
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<222> (75)..(81)
<223> XhoI restriction site
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<222> (98)..(114)
<223> cds first six amino acids of human serum albumin

<400> 30
tcagggatcc aagcttccgc caccatgaag tgggtaacct ttatttccct tctttttctc 60

tttagctcgg cttactcgag gggtgtgttt cgtcgagatg cacacaagag tgag 114

<210> 31
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<212> DNA
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<223> reverse primer useful for generation of
PC4:HSA albumin fusion VECTOR
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<223> Asp718 restriction site
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<223> EcoRI restriction site
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<223> reverse complement of stop codon

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<222> (18)..(43)
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<400> 31
gcagcggtac cgaattcggc gcgccttata gcctaaggc agc 43

<210> 32
<211> 46
<212> DNA
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<223> forward primer useful for inserting Therapeutic
protein into pC4:HSA vector
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<223> reverse primer useful for inserting Therapeutic protein into pC4:HSA vector

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1 5 10 15

<210> 35
<211> 22
<212> PRT
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<221> signal
<223> Synthetic signal peptide

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1 5 10 15

Trp Ala Pro Ala Arg Gly
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<210> 36
<211> 23
<212> DNA
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<400> 37
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<210> 39
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<400> 39
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<210> 40
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<210> 42
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<210> 43
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<210> 44
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<400> 44
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<210> 45
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<400> 45
tgaggagacg gtgaccgtgg tccc 24

<210> 46
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<210> 47
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<210> 48
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<210> 52
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<210> 53
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<210> 54
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<223>Linker peptide that may be used to join VH and VL domains in an scFv.

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tctcccggac tcctgaggtc acatgcgtgg tggtggacgt aagccacgaa gaccctgagg    180

tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca aagccgcggg    240

aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg caccaggact    300

ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca acccccatcg    360

agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac accctgcccc    420

catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc aaaggcttct    480

atccaagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac aactacaaga    540

ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag ctcaccgtgg    600

acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggctctgc    660

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gactctagag gat                                                       733


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<223> membrane proximal motif of class 1 cytokine receptors
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<223> Xaa equals any

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Trp Ser Xaa Trp Ser
  1               5

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site (GAS) containing promoter element

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cccgaaatat ctgccatctc aattag 86

<210> 76
<211> 27
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<400> 76
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<221> misc_feature
<223> Synthetic GAS-SV40 promoter sequence

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aaatatctgc catctcaatt agtcagcaac catagtcccg cccctaactc cgcccatccc 120

gcccctaact ccgcccagtt ccgcccattc tccgccccat ggctgactaa ttttttttat 180

ttatgcagag gccgaggccg cctcggcctc tgagctattc cagaagtagt gaggaggctt 240

ttttggaggc ctaggctttt gcaaaaagct t 271

<210> 78
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<223> primer useful for generation of a EGR/SEAP reporter construct

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<221> primer_bind

<223> primer useful for generation of a EGR/SEAP reporter construct

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<210> 80
<211> 12
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<221> misc_binding
<223> NF-KB binding site

<400> 80
ggggactttc cc 12

<210> 81
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<221> primer_bind
<223> forward primer useful for generation of a vector containing the NF-KB promoter element

<400> 81
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ccatctcaat tag 73

<210> 82
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<223> Synthetic NF-KB/SV40 promoter

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caattagtca gcaaccatag tcccgcccct aactccgccc atcccgcccc taactccgcc 120

cagttccgcc cattctccgc cccatggctg actaattttt tttatttatg cagaggccga 180

ggccgcctcg gcctctgagc tattccagaa gtagtgagga ggcttttttg gaggcctagg 240

cttttgcaaa aagctt 256

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. 6,946,134 B1 Page 1 of 39

APPLICATION NO.: 09/833,111

ISSUE DATE: September 20, 2005

INVENTOR(S): Craig A. Rosen, William A. Haseltine

It is hereby certified that an error or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Under item (60) (Related U.S. Application Data) of the title page, delete the text beginning with "Provisional application No. 60/256,931" to and ending "provisional application No. 60/229,358, filed on Apr. 12, 2000."

Under item (57) (ABSTRACT) of the title page, "disordrs" should read --disorders--.

On page 2, column 1, in the 8th reference from the bottom, "WO WO97/24445 *10/1997" should read --WO WO 97/24445 *7/1997--.

Under item (56) (References Cited) of the title page and under FOREIGN PATENT DOCUMENTS beginning on page 1, insert --WO WO 98/49296 5/1998--.

On page 2, column 2, in the 10th reference under OTHER PUBLICATIONS (Armstrong, J.D., et al.,), "(199)" should read --(1990)--.

On page 3, column 2, in the 13th reference (Bian, Z., et al.,), "78:355-344" should read --78:335-344--.

On page 4, column 1, in the 4th reference (Bolognesi, D.P., et al.,), "1233-1234" should read --246(4935):1233-1234--.

On page 5, column 1, in the 9th reference (Cunningham, B.C. et al.,), "245:821-825" should read --254:821-825--.

On page 5, column 1, in the 15th reference (Dedieu, J-F., et al.,), "*Journal of Virogy*" should read --*Journal of Virology*--.

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On page 9, column 1, in the 17th reference (Lewis, C., et al.,), "Dysfunctoin" should read --Dysfunction--.

On page 12, column 2, in the 17th reference, "Simoes, S., et a.," should read --Simoes, S., et al.,--.

On page 13, column 1, in the 11th reference, "Sotomayer" should read --Sotomayor--, and "77:19-16" should read --77:19-26--.

On page 14, column 1, in the 9th reference (Vorumn, H., et al.,), "19:1793-1802" should read --*Electrophoresis* 19:1793-1802--.

In the Specification:

Col. 1, line 3, delete the text beginning with "This application" to and ending "in its entirety." in col. 1, line 8.

Col. 267, line 18, "NO:36)." should read --NO:72).--.

Col. 418, line 33, "ID NO: 36)" should read --ID NO: 73)--.

Col. 439, line 24, "(SEQ ID NO: 37)" should read --(SEQ ID NO: 74)--.

Col. 440, line 46, "(SEQ ID NO: 38)" should read --(SEQ ID NO: 75)--.

Col. 440, line 50, "39)" should read --76)--.

Col. 440, line 67, "NO: 40)" should read --NO: 77)--.

Col. 443, line 5, "(SEQ ID NO: 41)" should read --(SEQ ID NO: 78)--.

Col. 443, line 7, "(SEQ ID NO: 42)" should read --(SEQ ID NO: 79)--.

Col. 445, line 24, "(SEQ ID NO: 43)" should read --(SEQ ID NO: 80)--.

Col. 445, line 29, "(SEQ ID NO: 44)" should read --(SEQ ID NO: 81)--.

Col. 445, line 34, "ID NO: 39)" should read --ID NO: 76)--.

Col. 445, line 50, "(SEQ ID NO: 45)" should read --(SEQ ID NO: 82)--.

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In the Claims:

Cancel claims 1-25, and insert the following claims:

1. An albumin fusion protein comprising a member selected from the group consisting of:

(a) a cerebus protein and albumin, wherein albumin comprises the amino acid sequence of SEQ ID NO:18;

(b) a cerebus protein and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf life of the cerebus protein compared to the shelf-life of the cerebus protein in an unfused state;

(c) a cerebus protein and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf life of the cerebus protein compared to the shelf-life of the cerebus protein in an unfused state, and further wherein the said fragment comprises the amino acid residues 1-387 of SEQ ID NO:18;

(d) a fragment of a cerebus protein and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment has a biological activity of the cerebus protein;

(e) a cerebus protein, or fragment thereof and albumin, or fragment thereof, of (a) to (d), wherein the cerebus protein, or fragment thereof, is fused to the N-terminus of albumin or the N-terminus of the fragment of albumin;

(f) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), wherein the cerebus protein or fragment thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment of albumin;

(g) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), wherein the cerebus protein or fragment thereof, is fused to the N- terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment of albumin;

(h) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), which comprises a first cerebus protein or fragment thereof and a second cerebus protein or fragment thereof, wherein said first cerebus protein or fragment thereof is different from said second cerebus protein or fragment thereof;

(i) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (h), wherein the cerebus protein or fragment thereof, is separated from the albumin or the fragment of albumin by a linker; and

(j) a cerebus protein or fragment thereof, and albumin or fragment thereof, of (a) to (i), wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

and further wherein R1 is cerebus protein or fragment thereof, L is linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or a fragment of albumin.

2. The albumin fusion protein of claim 1, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the cerebus protein or fragment thereof, in an unfused state.

3. The albumin fusion protein of claim 1, wherein the in vitro biological activity of the cerebus protein or fragment thereof, fused to albumin, or fragment thereof, is greater than the in vitro biological activity of the cerebus protein or fragment thereof, in an unfused state.

4. The albumin fusion protein of claim 1, wherein the in vivo biological activity of the cerebus protein or fragment thereof, fused to albumin, or fragment thereof, is greater than the in vivo biological activity of the cerebus protein or fragment thereof, in an unfused state.

5. An albumin fusion protein comprising a cerebus protein or fragment thereof, inserted into an albumin, or fragment thereof, comprising the amino acid sequence of SEQ ID NO:18 or fragment thereof.

6. An albumin fusion protein comprising a cerebus protein or fragment thereof, inserted into an albumin, or fragment thereof, comprising an amino acid sequence selected from the group consisting of:

(a) amino acid residues 54 to 61 of SEQ ID NO:18;
(b) amino acid residues 76 to 89 of SEQ ID NO:18;
(c) amino acid residues 92 to 100 of SEQ ID NO:18;
(d) amino acid residues 170 to 176 of SEQ ID NO:18;
(e) amino acid residues 247 to 252 of SEQ ID NO:18;
(f) amino acid residues 266 to 277 of SEQ ID NO:18;
(g) amino acid residues 280 to 288 of SEQ ID NO:18;
(h) amino acid residues 362 to 368 of SEQ ID NO:18;
(i) amino acid residues 439 to 447 of SEQ ID NO:18;
(j) amino acid residues 462 to 475 of SEQ ID NO:18;
(k) amino acid residues 478 to 486 of SEQ ID NO:18; and
(l) amino acid residues 560 to 566 of SEQ ID NO:18.

7. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the shelf-life of the cerebus protein or fragment thereof, as compared to the shelf-life of the cerebus protein or fragment, in an unfused state.

8. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the shelf-life of the cerebus protein or fragment thereof, as compared to the shelf-life of the cerebus protein or fragment, in an unfused state.

9. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vitro biological activity of the cerebus protein or fragment thereof, fused to albumin as compared to the in vitro biological activity of the cerebus protein or fragment, in an unfused state.

10. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vitro biological activity of the cerebus protein or fragment thereof, fused to albumin as compared to the in vitro biological activity of the cerebus protein or fragment, in an unfused state.

11. The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vivo biological activity of the cerebus protein or fragment thereof, fused to albumin compared to the in vivo biological activity of the cerebus protein or fragment, in an unfused state.

12. The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vivo biological activity of the cerebus protein or fragment thereof, fused to albumin compared to the in vivo biological activity of the cerebus protein or fragment, in an unfused state.

13. The albumin fusion protein of any one of claims 1-12, which is non-glycosylated.

14. The albumin fusion protein of any one of claims 1-12, which is expressed in yeast.

15. The albumin fusion protein of claim 14, wherein the yeast is glycosylation deficient.

16. The albumin fusion protein of claim 14, wherein the yeast is glycosylation and protease deficient.

17. The albumin fusion protein of any one of claims 1-12, which is expressed by a mammalian cell.

18. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

19. The albumin fusion protein of any one of claims 1-12, wherein the albumin fusion protein further comprises a secretion leader sequence.

20. A composition comprising the albumin fusion protein of any one of claims 1-12 and a pharmaceutically acceptable carrier.

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21. A kit comprising the composition of claim 20.

22. A method of extending the shelf life of a cerebus protein or fragment thereof, comprising the step of fusing the cerebus protein or fragment thereof, to albumin, or fragment thereof, sufficient to extend the shelf-life of the cerebus protein or fragment thereof, compared to the shelf-life of the cerebus protein, or fragment thereof in an unfused state.

23. A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-12.

24. A vector comprising the nucleic acid molecule of claim 27.

25. A host cell comprising the nucleic acid molecule of claim 28.

In the Sequence Listing:

Delete the Sequence Listing beginning in Col. 465, beginning with the text "<160> NUMBER OF SEQ ID NOS: 72" to and ending "<400> SEQUENCE: 72

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in Col. 505 and insert the following Sequence Listing:

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<213> Artificial Sequence
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<221> primer_bind
<223> primer useful to clone human growth hormone cDNA

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<221> misc_structure
<223> synthetic oligonucleotide used to join DNA fragments
with non-cohesive ends.

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<210> 5
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gaa aat ttc aaa gcc ttg gtg ttg att gcc ttt gct cag tat ctt cag   96
Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
             20                  25                  30

cag tgt cca ttt gaa gat cat gta aaa tta gtg aat gaa gta act gaa   144
Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
         35                  40                  45

ttt gca aaa aca tgt gtt gct gat gag tca gct gaa aat tgt gac aaa   192
Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
     50                  55                  60

tca ctt cat acc ctt ttt gga gac aaa tta tgc aca gtt gca act ctt   240
Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 65                  70                  75                  80

cgt gaa acc tat ggt gaa atg gct gac tgc tgt gca aaa caa gaa cct   288
Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
                 85                  90                  95
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gag aga aat gaa tgc ttc ttg caa cac aaa gat gac aac cca aac ctc   336
Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
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ccc cga ttg gtg aga cca gag gtt gat gtg atg tgc act gct ttt cat   384
Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
        115                 120                 125

gac aat gaa gag aca ttt ttg aaa aaa tac tta tat gaa att gcc aga   432
Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
    130                 135                 140

aga cat cct tac ttt tat gcc ccg gaa ctc ctt ttc ttt gct aaa agg   480
Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145                 150                 155                 160

tat aaa gct gct ttt aca gaa tgt tgc caa gct gct gat aaa gct gcc   528
Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
                165                 170                 175

tgc ctg ttg cca aag ctc gat gaa ctt cgg gat gaa ggg aag gct tcg   576
Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
            180                 185                 190

tct gcc aaa cag aga ctc aaa tgt gcc agt ctc caa aaa ttt gga gaa   624
Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
        195                 200                 205

aga gct ttc aaa gca tgg gca gtg gct cgc ctg agc cag aga ttt ccc   672
Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
    210                 215                 220

aaa gct gag ttt gca gaa gtt tcc aag tta gtg aca gat ctt acc aaa   720
Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225                 230                 235                 240

gtc cac acg gaa tgc tgc cat gga gat ctg ctt gaa tgt gct gat gac   768
Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
                245                 250                 255

agg gcg gac ctt gcc aag tat atc tgt gaa aat cag gat tcg atc tcc   816
Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
            260                 265                 270

agt aaa ctg aag gaa tgc tgt gaa aaa cct ctg ttg gaa aaa tcc cac   864
Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
        275                 280                 285

tgc att gcc gaa gtg gaa aat gat gag atg cct gct gac ttg cct tca   912
Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
    290                 295                 300
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tta gct gct gat ttt gtt gaa agt aag gat gtt tgc aaa aac tat gct   960
Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305                 310                 315                 320

gag gca aag gat gtc ttc ctg ggc atg ttt ttg tat gaa tat gca aga   1008
Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
                325                 330                 335

agg cat cct gat tac tct gtc gtg ctg ctg ctg aga ctt gcc aag aca   1056
Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
            340                 345                 350

tat gaa acc act cta gag aag tgc tgt gcc gct gca gat cct cat gaa   1104
Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
        355                 360                 365

tgc tat gcc aaa gtg ttc gat gaa ttt aaa cct ctt gtg gaa gag cct   1152
Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
    370                 375                 380

cag aat tta atc aaa caa aac tgt gag ctt ttt gag cag ctt gga gag   1200
Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385                 390                 395                 400

tac aaa ttc cag aat gcg cta tta gtt cgt tac acc aag aaa gta ccc   1248
Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
                405                 410                 415

caa gtg tca act cca act ctt gta gag gtc tca aga aac cta gga aaa   1296
Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
            420                 425                 430

gtg ggc agc aaa tgt tgt aaa cat cct gaa gca aaa aga atg ccc tgt   1344
Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
        435                 440                 445

gca gaa gac tat cta tcc gtg gtc ctg aac cag tta tgt gtg ttg cat   1392
Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                 455                 460

gag aaa acg cca gta agt gac aga gtc aca aaa tgc tgc aca gag tcc   1440
Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                 470                 475                 480

ttg gtg aac agg cga cca tgc ttt tca gct ctg gaa gtc gat gaa aca   1488
Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
                485                 490                 495

tac gtt ccc aaa gag ttt aat gct gaa aca ttc acc ttc cat gca gat   1536
Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
            500                 505                 510
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ata tgc aca ctt tct gag aag gag aga caa atc aag aaa caa act gca   1584
Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
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ctt gtt gag ctt gtg aaa cac aag ccc aag gca aca aaa gag caa ctg   1632
Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
    530                 535                 540

aaa gct gtt atg gat gat ttc gca gct ttt gta gag aag tgc tgc aag   1680
Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                 550                 555                 560

gct gac gat aag gag acc tgc ttt gcc gag gag ggt aaa aaa ctt gtt   1728
Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
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Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
         35                  40                  45

Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
     50                  55                  60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
 65                  70                  75                  80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
                 85                  90                  95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
            100                 105                 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
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Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
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Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145                 150                 155                 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
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Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
            180                 185                 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
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Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
    210                 215                 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225                 230                 235                 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
                245                 250                 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
            260                 265                 270

Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
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Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
    290                 295                 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
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Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
                325                 330                 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
            340                 345                 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
        355                 360                 365

Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
    370                 375                 380

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
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Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
                405                 410                 415
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Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
            420                 425                 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
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Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                 455                 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                 470                 475                 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
                485                 490                 495

Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
            500                 505                 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
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Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
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Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                 550                 555                 560

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site in pPPC0006

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Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
901 New York Avenue, N.W.
Washington, D.C. 20001-4413

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<221> misc feature
<222> (49)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (50)
<223> n equals a,t,g, or c

Finnegan, Henderson, Farabow,
Garrett & Dunner, L.L.P.
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<220>
<221> misc feature
<222> (51)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (52)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (53)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (54)
<223> n equals a,t,g, or c
<220>
<221> misc feature
<222> (55)
<223> n equals a,t,g, or c

<400> 33
agtcccatcg atgagcaacc tcactcttgt gtgcatcnnn nnnnnnnnnn nnnnn 55

<210> 34
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<221> signal
<223> Stanniocalcin signal peptide

<400> 34
Met Leu Gln Asn Ser Ala Val Leu Leu Leu Val Ile Ser Ala Ser Ala
1 5 10 15

<210> 35
<211> 22
<212> PRT
<213> Artificial Sequence
<220>
<221> signal
<223> Synthetic signal peptide

<400> 35
Met Pro Thr Trp Ala Trp Trp Leu Phe Leu Val Leu Leu Leu Ala Leu
1 5 10 15

Trp Ala Pro Ala Arg Gly
20

<210> 36
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate VH forward primer useful for amplifying human VH domains

<400> 36
caggtgcagc tggtgcagtc tgg 23

<210> 37
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate VH forward primer useful for amplifying human VH domains

<400> 37
caggtcaact taagggagtc tgg 23

<210> 38
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate VH forward primer useful for amplifying human VH domains

<400> 38
gaggtgcagc tggtggagtc tgg 23

<210> 39
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate VH forward primer useful for amplifying human VH domains

<400> 39
caggtgcagc tgcaggagtc ggg 23

<210> 40
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate VH forward primer useful for amplifying human VH domains

<400> 40
gaggtgcagc tgttgcagtc tgc 23

<210> 41
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate VH forward primer useful for amplifying human VH domains

<400> 41
caggtacagc tgcagcagtc agg 23

<210> 42
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate JH reverse primer useful for amplifying human VH domains

<400> 42
tgaggagacg gtgaccaggg tgcc 24

<210> 43
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate JH reverse primer useful for amplifying human VH domains

<400> 43
tgaagagacg gtgaccattg tccc 24

<210> 44
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate JH reverse primer useful for amplifying human VH domains

<400> 44
tgaggagacg gtgaccaggg ttcc 24

<210> 45
<211> 24
<212> DNA
<213> Artificial Sequence
<220>

<221>primer_bind
<223>Degenerate JH reverse primer useful for amplifying human VH domains

<400> 45
tgaggagacg gtgaccgtgg tccc 24

<210> 46
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 46
gacatccaga tgacccagtc tcc 23

<210> 47
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 47
gatgttgtga tgactcagtc tcc 23

<210> 48
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 48
gatattgtga tgactcagtc tcc 23

<210> 49
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 49
gaaattgtgt tgacgcagtc tcc 23

<210> 50

<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 50
gacatcgtga tgacccagtc tcc 23
<210> 51
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 51
gaaacgacac tcacgcagtc tcc 23

<210> 52
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vkappa forward primer useful for amplifying human VL domains

<400> 52
gaaattgtgc tgactcagtc tcc 23

<210> 53
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 53
cagtctgtgt tgacgcagcc gcc 23

<210> 54
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 54
cagtctgccc tgactcagcc tgc 23

<210> 55
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 55
tcctatgtgc tgactcagcc acc 23

<210> 56
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 56
tcttctgagc tgactcagga ccc 23

<210> 57
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 57
cacgttatac tgactcaacc gcc 23

<210> 58
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 58
caggctgtgc tcactcagcc gtc 23

<210> 59
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Vlambda forward primer useful for amplifying human VL domains

<400> 59
aattttatgc tgactcagcc cca 23

<210> 60
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221>primer_bind
<223>Degenerate Jkappa reverse primer useful for amplifying human VL domains

<400> 60
acgtttgatt tccaccttgg tccc 24

<210> 61
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jkappa reverse primer useful for amplifying human VL domains

<400> 61
acgtttgatc tccagcttgg tccc 24

<210> 62
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jkappa reverse primer useful for amplifying human VL domains

<400> 62
acgtttgata tccactttgg tccc 24

<210> 63
<211> 24
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jkappa reverse primer useful for amplifying human VL domains

<400> 63
acgtttgatc tccaccttgg tccc 24

<210> 64
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<221>primer_bind
<223>Degenerate Jkappa reverse primer useful for amplifying human VL domains

<400> 64
acgtttaatc tccagtcgtg tccc 24

<210> 65
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 65
cagtctgtgt tgacgcagcc gcc 23

<210> 66
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 66
cagtctgccc tgactcagcc tgc 23

<210> 67
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 67
tcctatgtgc tgactcagcc acc 23

<210> 68
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 68
tcttctgagc tgactcagga ccc 23

<210> 69

<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 69
cacgttatac tgactcaacc gcc 23

<210> 70
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 70
caggctgtgc tcactcagcc gtc 23

<210> 71
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<221>primer_bind
<223>Degenerate Jlambda reverse primer useful for amplifying human VL domains

<400> 71
aattttatgc tgactcagcc cca 23

<210> 72
<211> 15
<212> PRT
<213> Artificial Sequence
<220>
<221>turn
<223>Linker peptide that may be used to join VH and VL domains in an scFv.

<400> 72
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 73
<211> 733
<212> DNA
<213> Homo sapiens

<400> 73
gggatccgga gcccaaatct tctgacaaaa ctcacacatg cccaccgtgc ccagcacctg 60

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aattcgaggg tgcaccgtca gtcttcctct tccccccaaa acccaaggac accctcatga    120

tctcccggac tcctgaggtc acatgcgtgg tggtggacgt aagccacgaa gaccctgagg    180

tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca aagccgcggg    240

aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg caccaggact    300

ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca acccccatcg    360

agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac accctgcccc    420

catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc aaaggcttct    480

atccaagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac aactacaaga    540

ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag ctcaccgtgg    600

acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat gaggctctgc    660

acaaccacta cacgcagaag agcctctccc tgtctccggg taaatgagtg cgacggccgc    720

gactctagag gat                                                       733


<210> 74
<211> 5
<212> PRT
<213> Artificial sequence
<220>
<221> misc_structure
<223> membrane proximal motif of class 1 cytokine receptors
<220>
<221> misc_feature
<222> (3)
<223> Xaa equals any

<400> 74
Trp Ser Xaa Trp Ser
  1               5

<210> 75
<211> 86
<212> DNA
<213> Artificial Sequence

<220>
<221> primer_bind
<223> forward primer useful for generation of a synthetic gamma activation
site (GAS) containing promoter element

<400> 75
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gcgcctcgag atttccccga aatctagatt tccccgaaat gatttccccg aaatgatttc 60

cccgaaatat ctgccatctc aattag 86

<210> 76
<211> 27
<212> DNA
<213> Artificial Sequence
<220>
<221> primer_bind
<223> reverse primer useful for generation of a synthetic gamma activation site (GAS) containing promoter element

<400> 76
gcggcaagct ttttgcaaag cctaggc 27

<210> 77
<211> 271
<212> DNA
<213> Artificial Sequence
<220>
<221> misc_feature
<223> Synthetic GAS-SV40 promoter sequence

<400> 77
ctcgagattt ccccgaaatc tagatttccc cgaaatgatt tccccgaaat gatttccccg 60

aaatatctgc catctcaatt agtcagcaac catagtcccg cccctaactc cgcccatccc 120

gcccctaact ccgcccagtt ccgcccattc tccgccccat ggctgactaa ttttttttat 180

ttatgcagag gccgaggccg cctcggcctc tgagctattc cagaagtagt gaggaggctt 240

ttttggaggc ctaggctttt gcaaaaagct t 271

<210> 78
<211> 32
<212> DNA
<213> Artificial Sequence
<220>
<221> primer_bind
<223> primer useful for generation of a EGR/SEAP reporter construct

<400> 78
gcgctcgagg gatgacagcg atagaacccc gg 32

<210> 79
<211> 31
<212> DNA
<213> Artificial Sequence
<220>
<221> primer_bind

<223> primer useful for generation of a EGR/SEAP reporter construct

<400> 79
gcgaagcttc gcgactcccc ggatccgcct c 31

<210> 80
<211> 12
<212> DNA
<213> Artificial Sequence
<220>
<221> misc_binding
<223> NF-KB binding site

<400> 80
ggggactttc cc 12

<210> 81
<211> 73
<212> DNA
<213> Artificial Sequence
<220>
<221> primer_bind
<223> forward primer useful for generation of a vector containing the NF-KB promoter element

<400> 81
gcggcctcga ggggactttc ccggggactt tccggggact ttccgggact ttccatcctg 60

ccatctcaat tag 73

<210> 82
<211> 256
<212> DNA
<213> Artificial Sequence
<220>
<221> misc_feature
<223> Synthetic NF-KB/SV40 promoter

<400> 82
ctcgagggga ctttcccggg gactttccgg ggactttccg ggactttcca tctgccatct 60

caattagtca gcaaccatag tcccgccccc aactccgccc atcccgcccc taactccgcc 120

cagttccgcc cattctccgc cccatggctg actaattttt tttatttatg cagaggccga 180

ggccgcctcg gcctctgagc tattccagaa gtagtgagga ggctttttg gaggcctagg 240

cttttgcaaa aagctt 256